

Serial No. 09/779,376
Filed: February 7, 2001

The Applicants request that the following amendments be made and that the remarks set forth thereafter be considered.

AMENDMENTS

Please amend the above-identified application as follows:

In the Claims:

~~Please cancel Claims 1-4, 6-8, 17-18, 24-25, and 27-29 without prejudice or disclaimer as drawn to non-elected inventions.~~

Please amend Claims 9, 10, 13, 14, 19, 21, 23 and 26.

Sub B5 9. (Amended) A method according to claim 5 or 26 wherein said removing comprises:
a) enzymatically adding a binding ligand to said target sequence;
b) binding a hybridization complex comprising said target sequence comprising said binding ligand to a binding partner immobilized on a solid support;
c) washing away unhybridized probes; and
d) eluting said probe off said solid support.

A1 10. (Amended) A method according to claim 5 or 26 wherein said removing is done using a double-stranded specific moiety.

A2 13. (Amended) A method according to claim 5 or 26 wherein said amplifying is done by:
a) hybridizing a first universal primer to said UUP;
b) providing a polymerase and dNTPs such that said first universal primer is extended;
c) hybridizing a second universal primer to said DUP;
d) providing a polymerase and dNTPs such that said second universal primer is extended; and
e) repeating steps a) through d).

14. (Amended) A method according to claim 5 or 26 wherein said array comprises:
a) a substrate with a patterned surface comprising discrete sites; and

PZ
b) a population of microspheres comprising at least a first subpopulation comprising a first capture probe and a second subpopulation comprising a second capture probe.

Sub B7A
19. (Amended) A method according to claim 5 or 26 further comprising providing a support on which the target sequence is immobilized.

PH
21. (Amended) A method according to claim 5 or 26, further comprising attaching said target sequence to a support.

AS
23. (Amended) A method according to claim 5 or 26 wherein said support is selected from the group consisting of paper, plastic and tubes.

Sub B8
26. (Amended) A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain comprising said detection position and a second target domain adjacent to said detection position, wherein said method comprises:

a) providing a support on which the target sequence is immobilized;
b) hybridizing a first ligation probe to said first target domain, said first ligation probe comprising:

i) an upstream universal priming site (UUP); and
ii) a first target-specific sequence; and

c) hybridizing a second ligation probe to said second target domain, said second ligation probe comprising:

i) a downstream universal priming site (DUP); and
ii) a second target-specific sequence comprising a first base at an interrogation position;

wherein if said first base is perfectly complementary to said nucleotide at said detection position a ligation complex is formed and wherein at least one of said first and second ligation probes comprises an adapter sequence;

d) removing non-hybridized first probes;

e) providing a ligase that ligates said first and second ligation probes to form a ligated probe;

f) amplifying said ligated probe to generate a plurality of amplicons;
g) contacting said amplicons with an array of capture probes; and
h) determining the nucleotide at said detection position.